Sustainable Hospitals Project

A Project of the Lowell Center for Sustainable Production, University of Massachusetts Lowell

PILOT STUDY OF ALTERNATIVES TO THE USE OF XYLENE IN A HOSPITAL HISTOLOGY LABORATORY

Summary

This work focuses on identifying and evaluating alternatives to xylene used in a hospital histology lab as a solvent and clearing agent.

Hospitals in the Boston area are subject to very strict limits for the amount of xylene that may be discharged as effluent into the Massachusetts Water Resource Authority (MWRA) sewer system. The hospital in this case study exceeded the 1.0 milligrams per liter (mg/l) xylene limit and it was determined that the source of xylene was the hospital's histology laboratories. As part of the corrective actions agreed upon by the hospital and the MWRA, the Sustainable Hospitals Project (SHP) of the University of Massachusetts Lowell Center for Sustainable Production was asked to facilitate resolution of the problem. The SHP's expertise is in helping healthcare facilities reduce environmental and occupational hazards.

Although this action resulted from a violation of the hospital's sewer use permit, many hospitals are pursuing xylene alternatives because of xylene's adverse health and safety characteristics and to reduce hazardous waste disposal. High levels of exposure to xylene can cause renal failure, respiratory failure, hemorrhages, and necrosis of the brain, liver, kidneys, and heart. Other effects of high level exposure include agitation, headaches, light-headedness, eye irritation, dysphasia, shivering, and respiratory tract irritation (Harbison 1998). Chronic effects of workers exposed to xylene have shown decreased peripheral nerve function (Ruijten, 2001). Xylene is also suspected of causing hearing loss and may result in other Central Nervous System symptoms (Harbison, 1998).

The hospital histology laboratory and the SHP worked together to:

- Identify where xylene is used in the histology departments
- Identify potential alternatives for xylene applications in the histology departments
- Select and pilot two alternative (i.e. xylene-free) products
- Document the pilot process as a case study to be used as a model for other histology labs

Two alternatives were evaluated in the laboratory. Overall, the alternatives appear to be a favorable alternative to xylene. There were a few applications in which xylene was preferable, but even so the hospital was able to considerably reduce its xylene use. The product that was ultimately selected proved to be a "drop in" alternative; that is, the histology processes and conditions of use were unchanged and the alternative product was easily incorporated into

the lab's operation. As with many new products, questions arose which made communication with the manufacturer's representative and other labs using the product instrumental to the product's acceptance and successful use.

Purpose and Scope

This case study describes the actions taken by the MWRA and a Boston area hospital in order to address the hospital's discharge of xylene from the histology laboratory to the sewer system. With the guidance of the SHP, an evaluation was conducted to understand where xylene was found in a hospital's histology lab and to identify and pilot xylene-free alternatives. The evaluation considered the environmental, health and safety, functional and process aspects of the alternative products.

Methods

At the outset of the project, it was recognized that the histology departments were the source of xylene in the effluent. Therefore the agreed upon project consisted of four elements:

- Identifying where in the histology departments xylene was used and its purpose and function
- Finding potential xylene-free alternative products for those histology applications currently using xylene
- Selecting and conducting a pilot evaluation of two alternative products in order to evaluate the effectiveness and feasibility, with regards to pathological quality and worker safety
- Documenting the project in a case study that can be used as a model for other histology labs

The SHP facilitated the execution of these project steps using the following methods:

1. Identify Xylene Use in a Histology Laboratory

A comprehensive and systematic evaluation of the laboratory processes, materials, products, jobs and tasks were conducted. This provided a concise map of the materials, methods and waste products, allowing identification of all xylene use and waste products in the lab. Methods included:

- Mapping of the processes performed in each step in the histology lab to identify the overall work flow, and all equipment associated with each process step;
- Mapping of the materials used in each process and the types of waste streams produced (e.g. liquid, air, solid, hazardous) and their destination (e.g. sink-sewer, hazardous waste drums, medically regulated biological waste, regular trash);
- Analysis of the tasks and work practices associated with each process step through job site observations and employee interviews;
- Review of existing environmental and occupational health and safety monitoring data, relevant controls, and applicable regulations; and
- Review of the management organizational structure and management programs, policies and procedures for the use and handling of xylene and other chemicals and for disposal of waste streams containing xylene.

2. Identify Xylene Alternatives

Chemicals that can be used to perform the functions of xylene in the histology laboratory but have less damaging effects on environmental health and safety were identified through a combination of the following methods: 1.) Literature and the internet search and review with respect to the use of xylene and alternative chemicals for histology operations. Identification of other hospital pilot studies and change processes evaluations; 2.) Preliminary studies at other histology laboratories at two other regional hospitals; 3.) Interviews conducted with manufacturers to discuss the applications and benefits of their alternative products; and 4.) Interviews with representatives from histology departments at other hospitals that have successfully implemented alternative chemicals to the use of xylene in their laboratories.

3. Pilot Two Alternative Products

Once the alternatives were identified, criteria were developed to determine which were the best xylene replacements. Methods were developed to pilot the xylene alternatives. This was done by:

1.) Reviewing the toxicological and environmental literature to identifying criteria for evaluating the alternatives and comparing them to xylene (i.e. Health effects, safety, environmental impacts, regulatory climate),

2.) Developing a pilot protocol based on a.) interviews with workers and pathologists and, b.) the review of laboratory management, pathology, and histology literature,

3.) Creating a data collection form to tabulate and consolidate the results of the pilot trials in a manner that could be used to compare the quality of the histological slides produced using xylene to those made with the xylene alternatives, and

4.) Implementing the pilot protocols to collect data for the chemical alternative comparisons table and documenting the pilot results in terms of diagnostic quality, environmental benefits, and economic benefits or consequences. Six department pathologists reviewed seven different tissue samples prepared using the alternative chemicals in a total of 22 different combinations to make a determination of diagnostic quality.

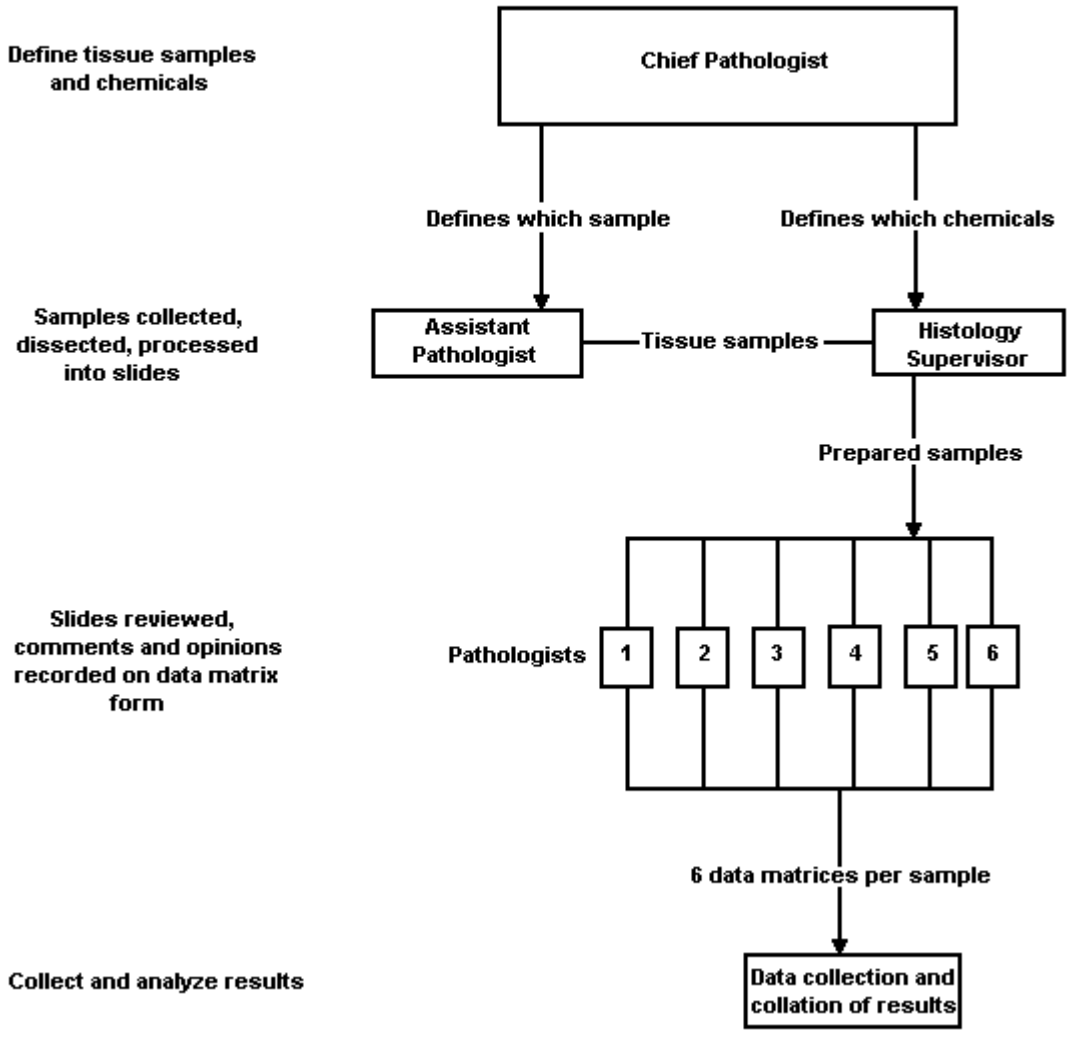
The chief pathologist instructed the assistant pathologist what samples to collect and then he communicated directly with the histology supervisor to assign which chemicals would be applied to these samples under what steps of the processes. As a result, the tissues were tested with various combinations of the alternative and xylene in different phases of the histology processes. Each of these combinations is identified on the data matrix, along with the quality results indication of the combinations.

During the evaluation the histology supervisor kept track of all the samples and processing chemical combinations. She was the only person in the lab who had the combination key.

None of the histology processes, chemical quantities, process times, process temperatures or any other combinations in the lab were altered during the pilot.

Once all of the tissue samples had been collected, dissected, and processed into slides, they were sent as a group to the pathologists to review. All six departmental pathologists participated in the slide review and provided input. All of the pathologists reviewing the samples were blind to the chemicals used to process the slides. Each doctor documented his or her comments and opinions regarding the quality of the slide on the data matrix. Sample evaluation process is given in Figure 1.

Figure 1. Samples evaluation



Results

Xylene Use

Comprehensive and systematic evaluations of the xylene-related lab processes, materials, products, jobs and tasks were conducted. Analysis of the steps and work practices associated with each process through job site observations and employee interviews. The processes performed in each step of the histology lab activities for slide preparation and processing are shown on Figure 2. Maps of the xylene use in each process and the types of waste streams produced (e.g. liquid, solid, hazardous) are shown in Figure 3.

Figure 2. Histology Process Steps

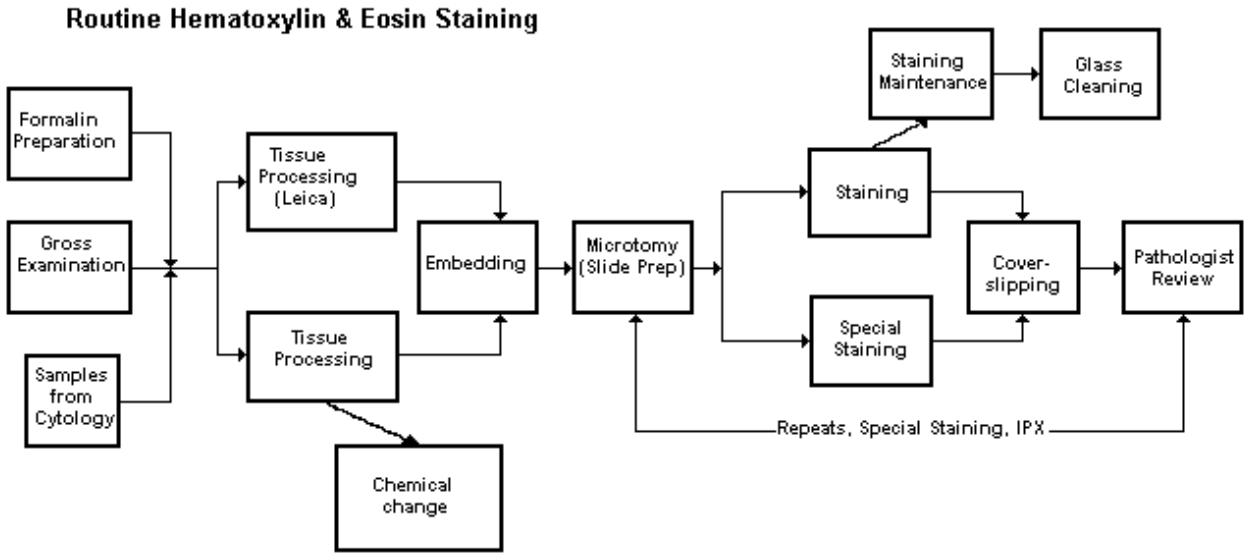
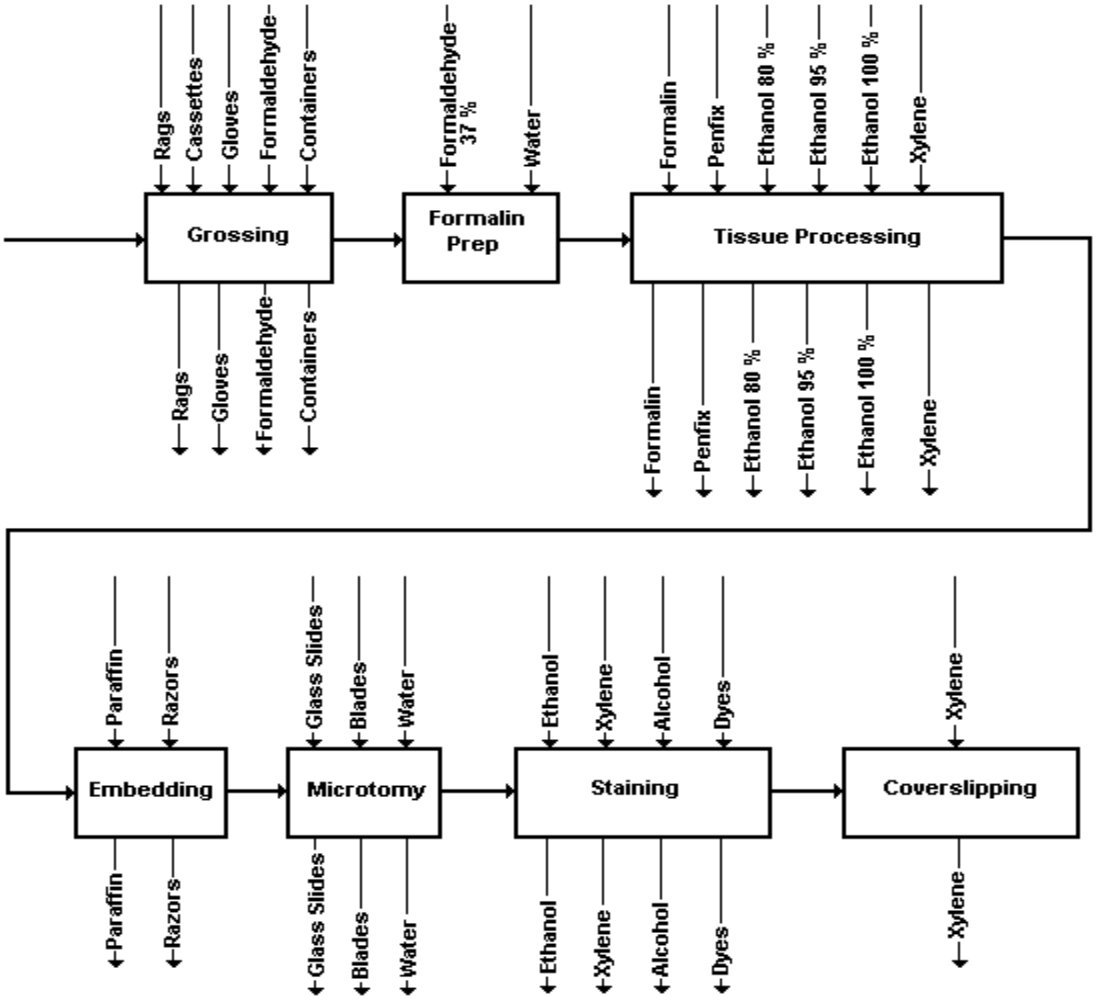


Figure 3. Histology Inputs/Outputs



Xylene Alternatives

Eventually two products were selected to be implemented in the pilot study, Histosolve and Clear-Rite 3. These were selected because of their reduced toxicological properties and because of the working experiences of other facilities using the products.

Pilot results

The most important indicator of the success of the pilot is the level of diagnostic quality as associated with the new methods and chemicals compared to xylene. In order for a new alternative chemical to be accepted by the pathologists it would have to provide either comparable or better diagnostic quality.

After there was consensus on which alternative to pilot in the laboratory, the Chief Pathologist made the determination about what tissues and tests to perform for the evaluation. A variety of about twenty different tissue specimens and types were collected initially. These

represented some of the more routine analyses and provided an initial indication of how the alternatives would work and whether there would be any problems encountered.

A challenge in this case study was that diagnostic quality could only be established by trained pathologists. Therefore the pilot was designed so that each of six doctors made their assessments individually and noted their comments and grade on a data matrix. This allowed the pathologists to evaluate qualitative characteristics of the slides and tests (for example in terms of good, poor, pale, well-defined borders, hazy, crisp, and muddy) and still provide a conclusion of acceptable or unacceptable. Their results were collected and collated to judge performance of the alternatives.

Table 1. Advantages and disadvantages of xylene and the alternatives in histology laboratory.

	Advantages	**Disadvantages**
Xylene	・Known product ・Produces high quality slides	・Noxious smell ・High toxicity ・Possible carcinogen ・Classified as hazardous waste due to flammability and toxicity ・Flammable ・Causes dermatitis, penetrates skin
HistoSolve	・Less Toxic ・Produces High Quality Slides ・Uses Same Procedures *Workers feedback* ・Acceptable consistency ・Did not affect/compromise stain quality ・Lack of offensive odor ・No process modifications required, including amount of solvent process time, process temperature ・Volume of waste and effluents unchanged	・Not Well Known ・Classified as hazardous waste due to flammability ・Slightly More Expensive *Workers feedback* ・Incompatible with currently used cover slipping media due to bubbles in slides[1] ・During cutting processes, it was noted that the tissues felt dry and brittle and it was hard to open wrinkled sections
ClearRite 3	・Less Toxic ・Produces Adequate Quality Slides ・Uses Same Procedures *Workers feedback* ・Did not affect/compromise stain quality ・Lack of offensive odor ・No process modifications required, including amount of solvent, process time, process temperature ・Volume of waste and effluents unchanged	・Not Well Known ・Classified as hazardous waste due to flammability ・Slightly More Expensive *Workers feedback* ・Very oily ・More difficult to work with than xylene. ・Incompatible with currently used cover slipping media due to bubbles in slides[1] ・During cutting processes it was noted that the tissues felt dry and brittle and it was hard to open wrinkled sections

[1] Conversations with other hospitals' laboratories indicated that they retained xylene for cover slipping.

The histology workers who processed the samples were also interviewed regarding the use of the alternative chemicals. They offered very helpful feedback on advantages and dis-advantages of both new and old chemicals. The workers comments are included in Table 1.

No significant problems were encountered in the implementation of the pilot study in the department. At the end of the pilot evaluation the group considered what might have been done differently.

- Each of the participants expressed a desire to have had more time to work on the study. Each of the participants estimated their time spent over the six-week study in the following list:
  Chief Pathologist – 15 hours
  Laboratory Manager – 30 hours
  Histology Supervisor – 36 hours
  Assistant Pathologist – 40 hours
  Pathologists – 2 hours each x 5 = 10 hours
  Purchasing Manager – 2 hours
- It was noted that the pass/fail method of ranking slides made it harder to assess the difference between slides prepared with different media. Most doctors passed most of the slides. A graded scale (for example, a quality rating of 1-5) would have provided a continuum of quality and an indicator of which slides resulted in better overall quality.
- There was general consensus about the importance of blind controls made with xylene as a basis against which to compare the alternatives. During the pilot, the doctors did not know the method of slide preparation (whether xylene, Histosolve, or Clear Rite was used). Adequate numbers of each alternative can ensure that quality trends or shortcomings are correctly recognized.

Conclusions

Advantages and disadvantages of xylene alternatives

Histosolve is less toxic than xylene and although it may have a higher vapor pressure (i.e. it evaporates more readily than xylene) than xylene the flashpoint (risk of fire) are not considerably different. If handled under adequate general ventilation the normal hazards and risks posed to workers were judged to be lower than when working with xylene.

Working with Histosolve in the lab resulted in no major differences in the operations and techniques used to process tissues. Problems with cover slipping can be avoided with the use of minimal quantities of xylene for these specific purposes. Thus, the overall volume of xylene used in the laboratory was reduced, although some was still required in the lab for special purposes. The cost of the Histosolve and Clear Rite are ~ $20/gal compared with ~$9/gal for xylene. Advantages and disadvantages of Xylene and the alternative chemicals are provided in Table 1.

Product quality

The Chief Pathologist indicated that he felt that the Histosolve alternative to xylene was comparable to xylene in the preparation of histology slides. The Chief Pathologist's opinions regarding the alternatives concur with analyses of the pilot study data collected from all six pathologists

Environmental health and safety benefits

Histosolve is comprised of a variety of isoalkanes (C9-C12). These isoalkanes exclude hexane and are not associated with the significant nervous system and respiratory irritant health effects of hexane. These chemicals are typically less toxic to both humans and biota than xylene. They do not tend to persist in the environment due to their high vapor pressures and they do not tend to bind or attach to sedentary environmental media. Histosolve has the disadvantage that it must be disposed of as a hazardous waste. This is because of its flammability, not toxicity.

The health benefits to workers using Histosolve in place of xylene are first characterized by the lack of noxious odors in the lab. Many workers are irritated by the noxious fumes in the workplace, even at low levels. Histosolve has no bad odors and does not seem to elicit irritation responses in lab workers.

Recommendations

In this pilot, the data indicated that for a large number of tissues and tests, the change to Histosolve is acceptable and feasible. The primary criterion, acceptable diagnostic quality, was achieved with the exception of the coverslipping process.

Recommendations for future work

- *Recognize that this was a small sample size and there is need to proceed cautiously with larger sample sizes and longer times*
- *Establish ongoing discussions with manufacturer and other hospitals to identify and/or resolve routine questions*
- *Proceed cautiously to other tissues not covered in this pilot*

References

Harbison, R. D., Ed. (1998). Hamilton & Hardy's industrial toxicology. St. Louis, Mosby.

Ruijten, M. (2001) "Neurobehavioral effects of long-term exposure to xylene and mixed organic solvents in shipyard spray painters." Neurological Toxicology 15: 613-620